PRESCRIPTION DRUG USER FEE ACT (PDUFA II) INFORMATION MANAGEMENT FIVE-YEAR PLAN

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1.0 BACKGROUND

The Prescription Drug User Fee Act of 1992 (PDUFA) provided FDA with increasing levels of resources for the review of human drug applications. That Act expired on September 30, 1997, but the FDA Modernization Act (FDAMA) of 1997 amended PDUFA and extended it through September 30, 2002 (PDUFA II). This extension will enable FDA to accomplish increasingly challenging goals over the next five years. PDUFA, as amended and extended by FDAMA, and with its new goals, is referred to as PDUFA II and its predecessor is now referred to as PDUFA I.

PDUFA II commits FDA to substantially faster review of some applications, to new goals for responding to industry requests for meetings and documenting outcomes of those meetings and for handling dispute resolutions, and to the transition to electronic receipt and review of applications by 2002. The new goals of PDUFA II are enormously challenging, diverse, and resource intensive. Major components of the review process will be accelerated further. Many of the goals will require the development and issuance of guidance documents. The development of infrastructure to provide the tools necessary to move to electronic application receipt and review will also be essential.

CBER, CDER, and the Office of Regulatory Affairs (ORA) have collaborated with the Office of the Chief Information Officer (OCIO) to develop an Agency-wide Information Management plan for investing PDUFA II information technology (IT) dollars in an Electronic Regulatory Submission and Review (ERSR) Program. This program and its component projects will support the transition from a largely paper-based regulatory submission and review environment to an electronic environment.

The FDA Chief Information Officer (CIO) also serves as the Associate Commissioner, Office of Information Resources Management (OIRM). In his role as Associate Commissioner, OIRM, responsibilities include the development, implementation and maintenance of the FDA wide-area network and entire telecommunications infrastructure, and the direct operational support for all offices and staffs within the Office of the Commissioner.

1.1 Purpose of Plan

The purpose of this document is to present how the ERSR projects fit into a single PDUFA IT Program. The Agency's PDUFA II Information Management Five-Year Plan describes the strategy for budgeting, executing, and managing PDUFA II IT funds during the period FY 1998 to FY 2002. This document provides a description of the PDUFA II ERSR Program, a milestone schedule for executing that program, and a description of the program management procedures and policies.

This document presents a budget plan and milestone schedule for major portions of the projects associated with the ERSR Program. The details and design specifications for several components will evolve over the next several months as the Centers refine their respective IT projects to better fit under the ERSR umbrella and to conform to FDAMA mandates. As a result, those programs will be reviewed again and this document will be updated to reflect the resulting budget and milestone details. In this regard, the PDUFA Information Management Five-Year Plan will serve as the baseline for monitoring and tracking ERSR projects over the next five years.

This document is intended to be a "living" document that provides a baseline for managing the expenditure of PDUFA II IT funds. The plan will be revisited annually to update forecasts, factor in actual expenses of previous years, and incorporate additional projects as they are identified. Mid-year progress reviews are also anticipated to assess progress toward planned milestones.

1.2 FDAMA and PDUFA II Program Goals

As part of PDUFA II, performance goals were set for the Center for Biologics Evaluation and Research (CBER) and the Center for Drug Evaluation and Research (CDER). Meeting these performance goals involves accelerating review of submissions (such as New Drug Applications (NDAs), Product License Applications (PLAs), Biologic License Applications (BLAs), efficacy supplements, and manufacturing supplements) over the next five years. The PDUFA performance goals also specifically call for the Agency to develop and update its information management infrastructure to allow, by fiscal year 2002, the paperless receipt and processing of Investigational New Drugs (INDs) and human drug applications, (as defined by PDUFA I), and related submissions.

The Agency's PDUFA II program provides funding to implement information technology initiatives that support the expedited approval of human drugs and biological products. FDAMA, in conjunction with the renewal of PDUFA, supports the Agency's transition from a largely paper-based regulatory submission and review environment to a new electronic paperless submission and review environment. This transition requires the Agency to fulfill three high-level objectives:

- Implement the ability to receive electronic submissions from regulated industry;
- Implement systems and procedures for reviewers to process submissions and generate review responses electronically; and
- Install any underlying or supporting technology necessary to handle this paradigm shift.

With regard to performance measures, the PDUFA II ERSR Program is in conformance with the Government Performance and Results Act (GPRA), FDAMA, the National Performance Review (implemented under the Agency's Performance Plan), the Paperwork Reduction Act, the Year 2000 Project, and Center-level strategic plans. Additionally, the Agency's commitment to implement Congressionally-mandated capital planning programs has driven the development of an integrated information management plan that achieves the performance goals of CDER and CBER in conjunction with ORA and the Agency's GPRA goals.

1.3 IT Goals Supporting FDAMA and PDUFA II Program Goals

FDAMA directs FDA to implement two major improvements related to IT:

1) Develop and update IT infrastructure to allow, by FY 2002, the paperless receipt and processing of INDs and NDAs/BLAs, and
2) Establish and maintain an information system to track the status and progress of each application or submission (including petitions, notifications, or other similar forms of requests) submitted to the Agency for action.

In addition to these IT-specific improvements, the Act directs FDA to meet new NDA/BLA review performance goals, adds new classification codes, and identifies new procedures (e.g., tracking of special protocols, resubmissions, meetings) which necessitate changes to existing information systems.

Activities to meet these FDAMA goals are augmented by Agency-wide efforts to meet IT goals established by the Agency's CIO. The CIO is leading the Agency's efforts to meet the challenge to maintain an aggressive application of new technology through an Agency-wide approach to investment selection and decision-making. Balance must be achieved between an increasing workload, unique Center business needs, and technology and information integration across the Agency. This balance requires review of Agency IT investments by FDA executive leadership, a sound technology base upon which these

applications will reside, and a viable set of Agency IT goals. To meet this challenge, the FDA is establishing an IT program to manage resources Agency-wide with the following goals:

- Facilitate information sharing within FDA by creating a common computing environment across the Agency;
- Reduce the regulatory burden on U.S. industry and the economy through the implementation of effective IT;
- Support the development of innovative technology solutions that support the regulatory process and improve the timely availability and ensure the safety of regulated products;
- Upgrade the FDA's ability to disseminate information to the public, academia, the scientific community, and industry through the evolution and sustainment of an integrated information environment throughout the Agency; and
- Create and sustain an effective IT Investment Review Process.

The objectives of the ERSR Program that support the Agency IT Goals are:

- Transition to a paperless, or near paperless, environment for program and administrative processes;
- Elimination of redundant or duplicate processes wherever feasible;
- Seamless, fast exchange of information within and across Centers and external to the Agency;
- Rigorous records management and document control, tracking, archiving;
- Robust electronic data interchange (EDI) capability for business and program data exchange;
- Standards-based information technology infrastructure; and
- Standards-based information repositories and data dictionaries.

1.4 Document Organization

This PDUFA II Information Management Five-Year Plan is organized as follows:

- Section 2.0 provides an overview of the PUDFA II ERSR Program and describes the functional areas of the program and their associated projects;
- Section 3.0 presents a master milestone schedule by functional area within ERSR; and
- Section 4.0 presents the process established for managing the ERSR Program.

A description of the major components of the ERSR Program for CDER and CBER are presented in Appendices A and B, respectively. Descriptions of the Agency/Cross-Cutting PDUFA II projects are provided in Appendix C. ERSR Program Costs are provided in Appendix D. A list of acronyms is included as Appendix E.

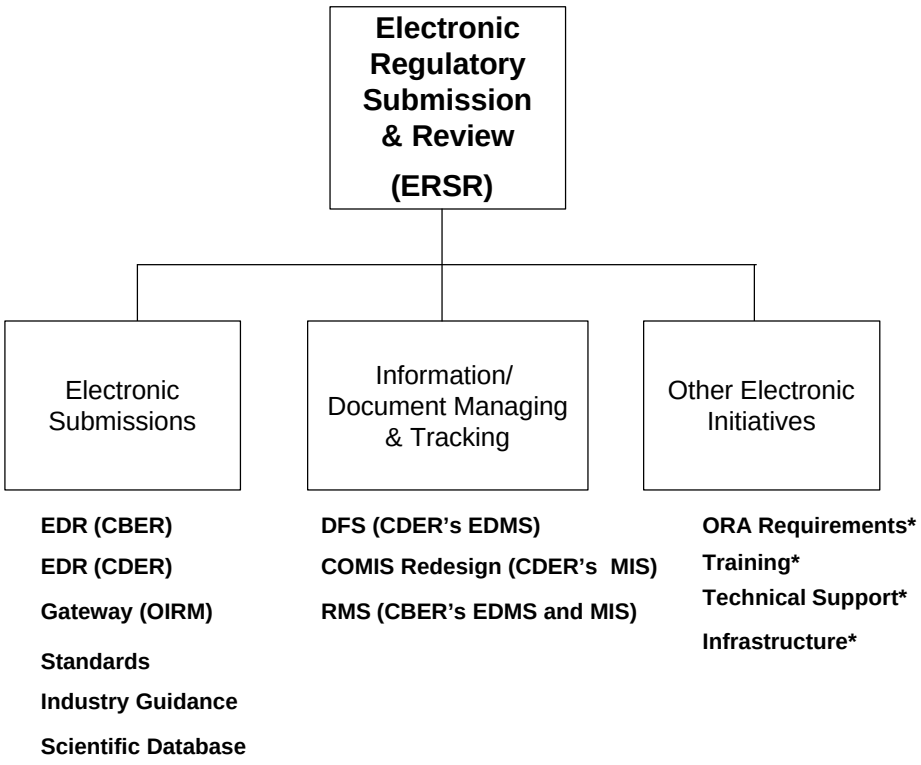
2.0 ELECTRONIC REGULATORY SUBMISSION AND REVIEW (ERSR) PROGRAM OVERVIEW

The ERSR Program supports the transition from a largely paper-based regulatory submission and review environment to an electronic environment. The ERSR Program is comprised of a variety of projects, each of which is designed to satisfy a different part of PDUFA. This overview of the ERSR Program includes descriptions of the current projects that are in different stages of development and implementation. Based on technological or business-related changes, it is expected that additional projects will be added or existing projects combined within the program during the five-year period covered by this plan.

The ERSR Program has been shared widely with industry since the mid-1990s via conferences and workshops sponsored by the Drug Information Association (DIA), collaboration with PhRMA's Regulatory Affairs Committee (RAC) and RAC's Electronic Regulatory Submissions (ERS) Working Group, participation in the International Conference on Harmonization (ICH) expert working groups, and presentations at industry trade meetings. Through this extensive collaboration within the Agency and with external parties, and as a result of subsequent voluntary pilots with regulated firms, the electronic submission of Case Report Tabulations (CRTs) and Case Report Forms (CRFs) in Portable Data Format (PDF) was implemented without major problems[1]. This early accomplishment under the ERSR Program demonstrates a successful partnership between the Agency and the industry it regulates. This partnership represents a critical success factor that will be key to achieving a paperless review by FY 2002.

The ERSR Program has been decomposed in an effort to simplify the management and enhance understanding for stakeholders. The projects within the ERSR Program are categorized in three functional areas: Electronic Submissions, Information/ Document Managing and Tracking, and Other Electronic Initiatives. The following paragraphs describe the functional areas and their associated projects and activities. Figure 1 shows the hierarchy of the three functional areas of ERSR and the projects and activities that currently comprise those areas.

[1] CRTs and CRFs are paper-intensive portions of a new drug application. These parts often make up approximately two-thirds of the paper submitted with NDAs.



*Activities cut across all three functional areas of the ERSR Program.

Figure 1

Figure 2 provides a conceptual view of the components of the ERSR Program. The explanation following Figure 2 presents the ERSR Program architecture and describes the configuration and information exchange between the various components of the ERSR Program.

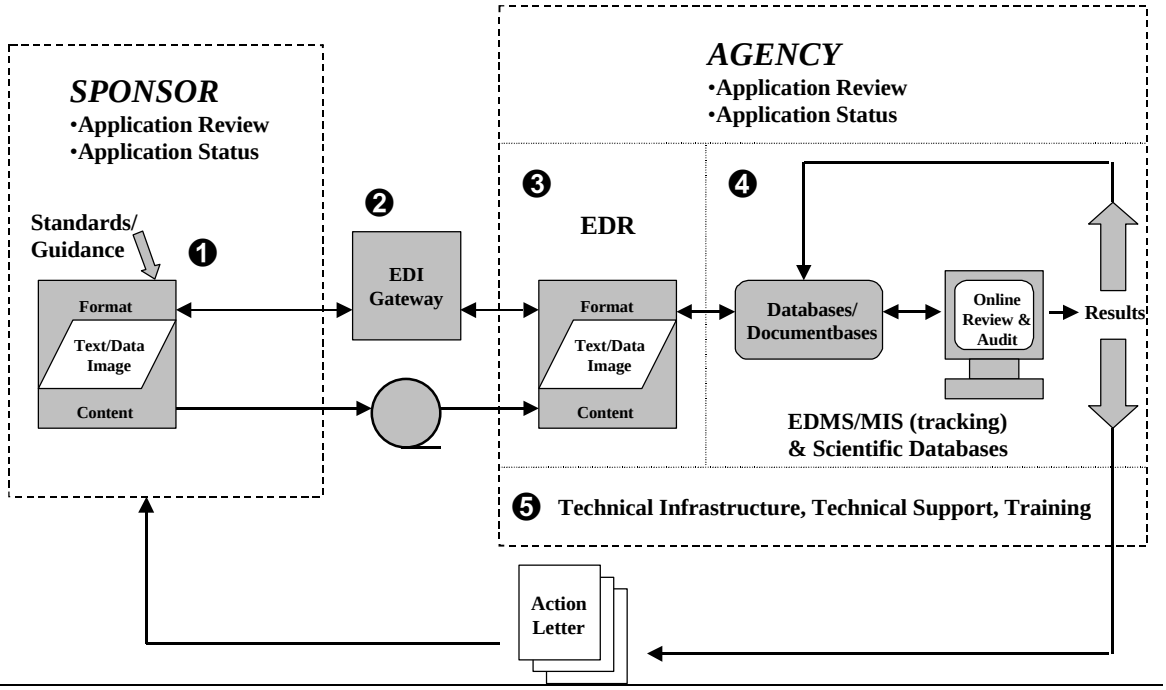


Figure 2

Guidance is prepared by the Agency so that pharmaceutical sponsors can submit their applications in conformance with applicable standards for format and content (❶). Electronic submissions that conform to the standards and guidance established are transmitted via the electronic Gateway or submitted via acceptable physical media (❷). The Electronic Document Room (EDR) accommodates the program area receipt, archive, and storage of these submissions (❸). Reviewers and field inspectors are able to operate in an electronic review environment with appropriate access to IND/BLA/NDA tracking data (Management Information System (MIS)) electronic submissions and related historical review documents and access to tools (Scientific Databases). Resulting reviews are stored, routed, and can be retrieved again at a later date (Electronic Document Management System) (❹). All aspects of the ERSR Program are supported by an infrastructure including standard hardware/software (e.g., desktops, network, office automation tools, servers, Internet/Intranet) and additional capabilities as needed, such as a secure e-mail package for communicating with regulated industry, field component review and inspection access, and analytical tools needed by reviewers for use with structured databases. In addition, there are foundational support aspects to the solution such as underlying technical architecture, training, and technical support (❺).

2.1 Electronic Submissions

The PDUFA II Program goals call for an electronic submission capability to be established by the year 2002. The success of the Electronic Submissions portion of ERSR is dependent upon the accurate and thorough definition of data and reporting standards for the format and content of regulatory submissions and the dissemination of guidance for industry to prepare submissions.

Standards - FDA is involved in several standards-related projects to define the format and content of regulatory submissions. The Agency actively participates in activities of the International Conference on Harmonization (ICH), which is an enormous science-driven initiative to curtail regulatory duplication by working towards a common worldwide drug and biologic registration package. The ICH M2 Expert Working Group (EWG) focuses on Electronic Standards for Transmission of Regulatory Information. The goal of M2 is to identify, evaluate, and recommend appropriate and relevant standards to facilitate the electronic transfer of regulatory information between industry authorities and among regulatory agencies. CDER serves as the Rapporteur for the M2 EWG and CBER is a participant. The ICH M4 EWG focuses on Common Technical Documents (CTD) for the technical content of sections of the NDA.

Industry Guidance – Upon establishment of the standards, FDA provides written guidance for industry to follow in preparing electronic submissions. Guidance documents are posted in FDA's public docket. Industry training is provided at technical workshops and IT conferences hosted by organizations such as DIA. In September 1997, guidance entitled "Archiving Submissions in Electronic Format – NDAs" was published, allowing the first electronic submissions to be received in CDER without an accompanying paper copy. This guidance covers only electronic CRFs and CRTs. However, CDER is in the process of expanding the guidance to cover electronic submission for archive of the remaining NDA sections, as well as other document types such as Abbreviated New Drug Applications (ANDAs) and Drug Master Files (DMFs). CBER and CDER are collaborating on marketing applications as well as INDs. CBER has taken the lead on preparing guidance for electronic submission of INDs and BLAs, and those guidance documents currently are under staff review. The development and completion of guidance documents serve as the foundation for enabling regulated industry to exchange electronic submissions with the Agency.

Electronic submissions that conform to the established standards and guidelines will be transmitted via an electronic gateway or submitted via acceptable physical media. Systems involved in the successful implementation of the electronic submission area include the Electronic Document Room and the Agency's Electronic Gateway. In addition, structured databases, reference guides, and analytical tools needed by reviewers to perform standard analytical processes on electronic submissions directly from the desktop are an important component of the electronic submission area.

Electronic Document Room (EDR) – CDER established an EDR in FY 1997 to accommodate the receipt, archive, and storage of electronic CRFs and CRTs for NDAs -- text images in PDF for archive. Submissions come in on one of several physical media types as defined in the industry guidance posted in the public docket. A comparable interim facility for e-INDs and BLAs was established in CBER. CBER will begin development of the full EDR pending a comprehensive requirements study that will be completed in September 1998. As part of its comprehensive requirements study, CBER

will evaluate CDER's EDR for the feasibility of having a single document room facility process electronic submissions for both CBER and CDER. Between September 1997 and May 1998, CBER received approximately 6 electronic submissions and CDER received 27 electronic submissions.

Electronic Gateway - The Gateway has been designed and developed to serve as an Agency-level central point for receipt of secure Electronic Data Interchange (EDI) submissions (via Internet). Its Release 1.0 design provides an ability to decrypt, authenticate, validate, and route information to the FDA Centers. Release 1.0 of the Gateway was implemented to support the electronic transmission of adverse event reports for CDER and CBER into the Adverse Event Reporting System (AERS). The current production release is "receipt only". Requirements for two-way exchange of data will be considered in later releases. Successive releases will implement pre-approval types of electronic submissions. Release 2.0 includes a requirements study involving representatives from CBER, CDER, ORA, and regulated industry. The scope of Release 2.0 will be determined upon completion of the study.

Scientific Databases - Scientific Databases include structured databases, reference guides, and analytical tools needed by reviewers to perform standard analytical processes on electronic submissions directly from the desktop. Previously, CDER introduced the Entry Validation Application (EVA) pilot for electronic structured submissions of bioequivalence data that accompany generic drug applications. This program was funded out of appropriations and now is being expanded for use with NDAs – specifically for Chemistry, Manufacturing and Controls (CMC) data and biopharmaceutics data. It is especially valuable for chemistry supplements and annual reports where information is additive over a number of years. The potential outcomes of structured databases include, but are not limited to: data integration, data standards, better information sharing and exchange, and better tools to facilitate the review. Other tools include the Chem-X system which allows users to search chemical structures in three-dimensional form while conducting a CMC review.

2.2 Information/Document Managing and Tracking

The Information/Document Managing and Tracking area of the ERSR Program focuses on 1) providing an automated means for creating, managing, and archiving internally-generated review documents and 2) tracking the status and progress of submissions submitted to the Agency for action, generating mandatory user fee reports, and enabling tracking of milestones and workload statistics for improved management accountability. These two areas of focus are categorized as Electronic Document Management System (EDMS) and Management Information System (MIS), respectively. The following paragraphs describe those two areas and their respective component projects.

Electronic Document Management System (EDMS) - EDMS provides an automated means for creating, managing, and archiving internally generated review documents as well as for electronic signature of those documents. EDMS consists of several components that are designed to provide an easy to use, automated means for accessing information, documents, and communications pertaining to the IND/BLA/NDA review process. The objective of EDMS is to improve, through the use of information technology, the way CBER and CDER 1) route documents for comment/approval/ audit/validation, 2) retrieve historical documents for reference, and 3) archive documents in an electronic repository.

Moreover, it may provide reviewers the capability to specify and route pertinent documents to ORA field staff.

In CDER, EDMS is performed by the Division Files System (DFS) that is currently operational in 10 new drug review divisions and offices and, upon completion, will support the needs of all new and generic drug review divisions.

In CBER, EDMS is performed by the Regulatory Management System (RMS), an integrated system for creating, managing and archiving internal review documents concerning a submission, as well as tracking the status of the submission. Portions of RMS are operational throughout the Center.

These systems are Center-specific due to differing business needs created by legislative statutes and mandates. However, both systems are being developed under the ERSR Program; therefore, the technical architecture for both is largely the same and consistent with the Agency's Information Systems Architecture (ISA) program. Further harmonization of systems depends heavily on the modification of current law and regulations.

Management Information System (MIS) - The MIS is the corporate database/application that is used to track status and progress of each submission (including petitions, notifications, or other similar forms of requests) submitted to the Agency for action. It is also used to generate mandatory user fee reports and to enable tracking of milestones and workload statistics for improved management accountability. The MIS is integrated with the EDMS to prevent data redundancies and ensure data integrity. Currently, a requirements analysis is being conducted to determine the feasibility of the MIS interfacing with other systems such as ORA's Field Accomplishments and Compliance Tracking System (FACTS) to provide and track status of assignments to ORA field staff.

In CDER this integration of MIS and EDMS is represented by the integration of the Corporate ORACLE Management Information System (COMIS) and DFS. In CBER, this integration is represented similarly by the RMS.

It is this integrated EDMS/MIS that will enable more timely application status information throughout the review (e.g., as each scientific discipline completes its review) in lieu of waiting until the entire review has been completed.

2.3 Other Electronic Initiatives

This functional area includes various activities associated with the technical infrastructure of the ERSR Program (e.g., acquiring, configuring, and implementing hardware and software). These often underlying activities support multiple projects and are coordinated with projects' functionality needs as appropriate. These items include standard hardware/software (e.g., desktops, network, office automation tools, servers, Internet/Intranet) needed to support the EDR, EDMS, MIS, and Scientific Databases. This functional area also includes additional capabilities as needed, such as a secure e-mail package for communicating with regulated industry and analytical tools needed by reviewers for use with structured databases. Other tools include library references such as the scientific Library Electronic Reference Network (LERN).

ORA Requirements

This functional area also includes addressing the needs for Center communication with ORA Field Offices. ORA's requirements will be integrated as appropriate with the ERSR-related functional capabilities developed in CBER and CDER. An analysis of the changes required to ORA's computing infrastructure is planned[2]. ORA envisions that they will need the capability to 1) provide each district office, each laboratory, some large resident posts on the network, and each regional office direct electronic access to the electronic documents maintained by CDER and 2) provide the ability to browse and search for the documents pre-authorized by CDER and download what they need when they need it. ORA does not require detailed access to CBER's BLA applications in the same context as in audits of CDER NDAs in accordance with CDER guidelines. One solution being considered is to provide a seamless dial-up capability to access the information needed by ORA and to have added electronic storage capability.

Funds have been included in the reserves for CBER and CDER and are earmarked for incorporating ORA requirements in their respective Centers. ORA must concur with the use of these funds before they are released.

The following table lists activities associated with "other electronic initiatives".

CBER	CDER	OIRM	ORA
- Perform technical integration – desktop development - Purchase software – SAS, BackOffice - Fund infrastructure costs associated with WOC I cabling, Network Hardware, NT Network Operating System (NOS), IIP Labor - Purchase personal computers and local peripherals - Upgrade to MS Office Pro 97	- Perform technical integration – desktop development - Purchase software – SAS, BackOffice - Accommodate ORACLE database requirements - Replace Imaging System - Contract for Imaging technical support - Purchase personal computers, local peripherals, and local software - Upgrade to MS Office Pro 97	- ISA and Central Infrastructure Support for PDUFA-related activities	- Fund interface with FACTS to Center systems as appropriate - Purchase electronic document management system software - Fund infrastructure costs associated with ISDN Circuits, NT servers, Hub, and other network hardware and cable - Purchase personal computers, laptops, and local peripherals - Upgrade to MS Office Pro 97

Infrastructure also includes the foundational support aspects of the ERSR Program which are common to CBER, CDER, and ORA's PDUFA II IT solution:

> *Technical Support* – Provides support to end users for hardware/software installation, software development, maintenance, and trouble shooting.
>
> *Training* – Covers provision of training for development staffs and end users sufficient to ensure qualified technical support to the ERSR Program and to allow reviewers to function in an electronic review environment.

[2] CDER and CBER are currently conducting a series of requirements gathering meetings with ORA program management and IT management to identify the functionality needs of the Field Offices. As ORA's needs are defined and CBER and CDER complete strategies for meeting those needs in their project planning, this document will be updated with appropriate milestones and schedule.

3.0 MASTER MILESTONE SCHEDULE

The schedule provided in this section represents the current plan, presented by functional area within ERSR, for accomplishing PDUFA II milestones over the next five years. This schedule does not include all milestones associated with the ERSR Program. Some activities are in the planning stages and, therefore, definite target completion dates are being formulated. As planning for these activities becomes more conclusive, this milestone schedule will be updated.

This schedule will be used to track progress toward meeting established milestone dates and will be updated regularly to include milestones as they are identified.

3.1 Schedule for Electronic Submissions

The following table presents milestones and associated target completion dates for activities involved with the electronic submission portion of the ERSR Program. This schedule is consistent with performance goals cited in FDAMA, the FY 2000 GPRA Performance Plan, and Center planning documents.

Functional Area	Milestones	Target Date
Electronic Submissions		
1. Standards	- ICH M2 Expert Working Group (EWG) for Electronic Standards for Transmission of Regulatory Information	Ongoing
	- ICH M4 EWG for Common Technical Documents (CTD) involving the technical content of sections of an NDA	2/2000
2. Provide industry guidance for electronic submissions	- Capability Electronic Submissions of CRFs and CRTs (partial NDA and PLA)	Completed
	- Full NDA (CDER)[3]	9/1999
	- ANDA (CDER)[4]	9/2000
	- Investigational New Drug Applications (IND) (CBER)	9/2000
	- Biologics License Application (CBER)	9/2001
	- All other document types (CDER and CBER)	9/2002
3. EDR	- Phase I – Accommodate E-CRFs and E-CRTs (CDER)	Completed
	- Phase I – Implement EDR (CBER)	9/1999
	- Phase II – Capability to accept full Electronic NDA (CDER)	9/1999
	- Phase II – Capability to accept full electronic BLAs (CBER)	9/2001
	- Phase III a – Capability to accept ANDAs (CDER)	9/2000
	- Phase III b – Capability to accept INDs (CBER)	9/2000
	- Phase IV – Capability to accept all other document types (CBER and CDER)	9/2002
4. Gateway	- Requirements Analysis (OIRM)	12/1998
	- Release 2.0 – Pending by Requirements Analysis (OIRM)	10/2000
	- Release 3.0 – Pending by Requirements Analysis (OIRM)	10/2001
	- Release 4.0 – Pending by Requirements Analysis (OIRM)	10/2002
5. Scientific Databases	- EVA for BA/BE data (CDER)	Completed
	- EVA for CMC and biopharmaceutics data piloted (CDER)	9/2000
	- Drug-Drug Interaction (CDER)	10/2002
	- Carcinogenicity (CDER)	10/2002
	- Chem-X (CDER)	9/1998

[3] GPRA goals state that the Agency will post guidance in the public docket for the full NDA in FY 1999.
[4] GPRA goals state that the Agency will post guidance for public comment for the full ANDA in FY 2000; ANDA guidance will be posted in the public docket in FY 2000.

3.2 Schedule for Information/Document Managing and Tracking

The following table presents milestones associated with the EDMS and MIS portions of the ERSR Program. Some activities are still in the planning stages and, therefore, definitive target completion dates are being formulated. As planning for these activities becomes more conclusive, this milestone schedule will be updated.

Functional Area	Milestones	Target Date
Information/Document Managing and Tracking		
1. EDMS	DFS Phase 1 (CDER) DFS Phase 2 (CDER) RMS 3.0 (CBER)	12/1997 9/1999 10/1999
2. MIS	COMIS Phase 1 (CDER) COMIS Phase 2 (CDER) COMIS Phase 3 (CDER) EES for BiMo (CDER) RMS 2.0[1] (CBER)	10/1999 5/2000 5/2001 10/2002 9-12/1998

[1] RMS Rollout: RMS 2.0 will be released coincident with the BLA final rule in the first quarter FY 1999. It will provide basic BLA tracking, as well as the IND tracking from RMS version 1.2. While the Biologics Regulatory Management System (BRMS) database will be maintained for analysis purposes, all active license applications in BRMS will be converted to the RMS 2.0 database, as well as the Document Accountability and Tracking System (DATS) replacement for DLS, the Lot Release System database (LRS), and the Blood Establishment Registration System database (BER). RMS 3.0, planned for the first quarter of FY 2000, will incorporate reviewer comments.

3.3 Other Electronic Initiatives

The following table presents milestones associated with the other electronic initiatives associated with the ERSR Program. These activities support multiple projects and are coordinated incrementally with functionality needs as appropriate.

Functional Area	Milestones	Target Date
Other Electronic Initiatives		
1. Technical Infrastructure	Technical Infrastructure	On-going (2)
2. Technical Support	Technical Support	As needed
3. Training	Training	As needed

(2) Dates are driven by implementation schedules for EDR, Scientific Databases, EDMS, and MIS.

3.4 Master Gantt Chart

Figure 3 provides a Gantt chart showing the target dates for ERSR milestones over the five-year PDUFA II period.

ID	Task Name
1	**Electronic Submissions**
2	**Standards**
3	ICH M2 Expert Working Group (EWG)
4	ICH M4 Expert Working Group (EWG)
5	**Industry guidance for Electronic Submissions**
6	Capability Electronic Submissions of CRFs and CRTs (partial NDA and PLA
7	Full NDA (CDER)
8	ANDA (CDER)
9	Investigational New Drug Applications (IND) (CBER)
10	Biologics License Application (CBER)
11	All other document types (CDER and CBER)
12	**Electronic Document Room**
13	Phase I - Accommodate E-CRFs and E-CRTs (CDER)
14	Phase I - Implement EDR (CBER)
15	Phase II - Capability to accept full Electronic NDA (CDER)
16	Phase II - Capability to accept full electronic BLAs (CBER)
17	Phase III a - Capability to accept ANDAs (CDER)
18	Phase III b - Capability to accept INDs (CBER and CDER)
19	Phase IV - Capability to accept all other document types (CBER and CDER
20	**EDI Gateway**
21	Requirements Analysis (OIRM)
22	Release 2.0 - TBD by Requirements Analysis (OIRM)
23	Release 3.0 - TBD by Requirements Analysis (OIRM)
24	Release 4.0 - TBD by Requirements Analysis (OIRM)
25	**Scientific Databases**
26	EVA for BA/BE data (CDER)
27	EVA for CMC and biopharmaceutics data piloted (CDER)
28	Drug-Drug Interact (CDER)
29	Carcinogenicity (CDER)
30	Chem-X (CDER)
32	**Information/Document Managing and Tracking**
33	**EDMS**
34	DFS Phase 1 (CDER)
35	DFS Phase 2 (CDER)
36	RMS 3.0 (CBER)
37	**MIS**
38	COMIS Phase 1 (CDER)
39	COMIS Phase 2 (CDER)
40	COMIS Phase 3 (CDER)
41	EES for BiMo (CDER)
42	RMS 2.0 (CBER)
44	**Other Electronic Initiatives**
45	Technical Infrastructure
46	Technical Support
47	Training

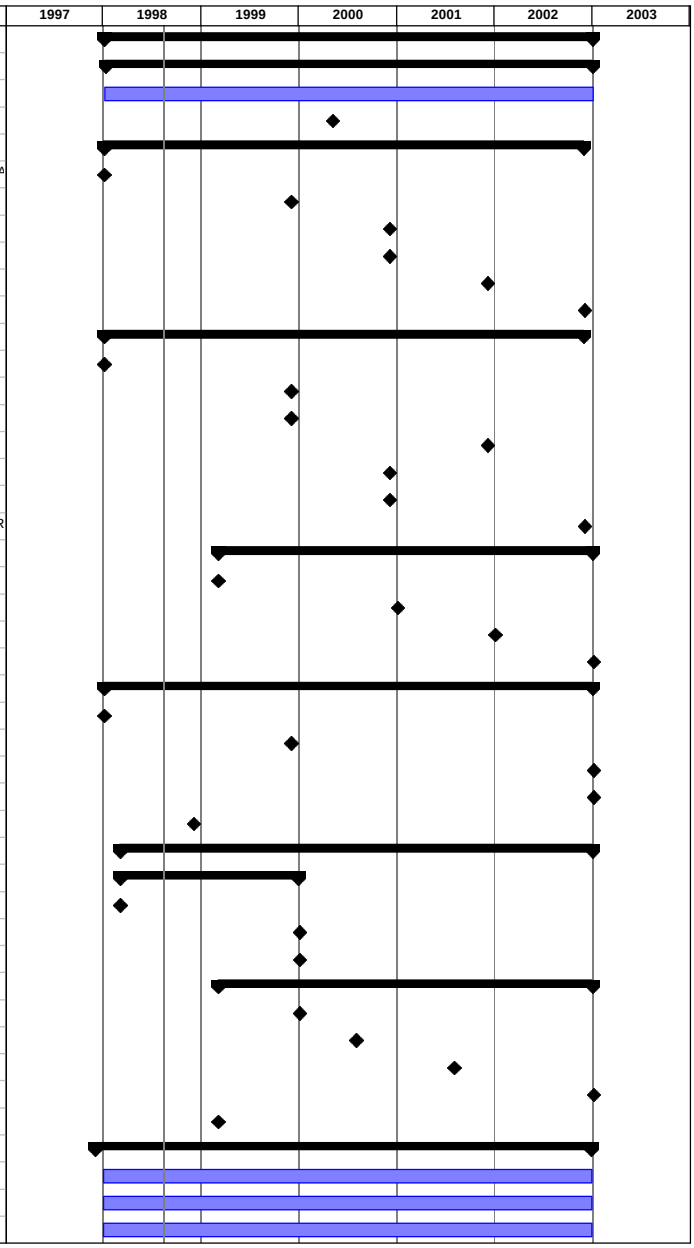


Figure 3

4 .0 PROGRAM MANAGEMENT

The Office of the CIO (OCIO) is responsible for ensuring that all PDUFA II IT investments support the Agency's common IT goals, fit into a common computing environment, and follow good IT management practices.

CBER, CDER, and ORA independently developed functional five-year spending plans. OCIO, in conjunction with an independent review of the individual spending plans, developed an Agency-level consolidated budget plan. The costs associated with that consolidated plan are presented in Appendix D.

Management of the ERSR Program will involve three integrated processes. First, ERSR projects will be reviewed for business and technical soundness through the IT Business Planning Process established by the Agency in accordance with the Clinger-Cohen Act of 1996. Second, the ERSR Program will be audited annually by an independent consultant who will work with the Centers/Offices to review and assess the economic soundness of PDUFA IT investments and monitor performance in meeting established milestones. Finally, during the initial independent review, funds for certain IT projects were placed in a "reserve" because these projects were considered to be in such a formative stage of their development as to preclude definite estimates of actual funding requirements. These reserve funds will be managed by a collaborative effort between the Centers/ORA, the OCIO, and the Office of Financial Management (OFM).

4.1 IT Business Planning Process

Consistent with Department of Health and Human Services (DHHS) policies and recent legislation, including the Clinger-Cohen Act, the Agency has developed a process to become more accountable for the economic and efficient management of IT and to implement a sound and integrated IT architecture.

In FY 1997, the FDA defined and implemented an information technology business planning (ITBP) process. This process, begun with an initial focus on selected high priority IT projects, was developed in close collaboration with senior Agency managers. Throughout 1998, senior Agency management remained engaged in the refinement and expansion of the process to include all major IT investments within the Agency.

An integral part of the FDA business planning process is the review of the major IT investments to ensure that they are achieving defined performance goals which support the Agency mission, in terms of the project plan (i.e., milestones and resources) and expected outcomes (e.g., programmatic improvements), and are compliant with standards defined by the Agency's information systems architecture (ISA).

In FY 1998, the ITBP process has been utilized to review all existing ERSR IT projects. The ITBP process required the sponsoring PDUFA II Centers/Offices to prepare business cases for their IT investments. A business case is a narrative document that provides a consistent format to capture information such as business need, IT solution, costs, schedule (milestones), and performance measures.

All PDUFA II information technology investments will continue to be reviewed through this ITBP process. One major component of the ITBP process is a review of investments by a Technical Review Board (TRB) composed of Information Resource Management (IRM) Directors from each of the Centers/Offices. The goal of the TRB is to assess Agency IT investments with regard to the technical soundness of the investment, the consistency of the IT solution with the Agency's ISA, and the potential redundancy of the investment with other Agency efforts. Once the TRB has completed its assessment and determined that there are no significant technical risks that could prevent successful implementation of the IT solution, the

members "credential" the investment. Though projects may be "credentialed" by the TRB, members may raise technical issues that must be addressed by project managers but do not preclude a project from proceeding.

Specific ERSR projects already reviewed and "credentialed" by the TRB include: CBER's Regulatory Management System (RMS), CDER's Electronic Document Room (EDR), CDER's Division File System (DFS), and OIRM's EDI Gateway. These projects will be provided immediate access to PDUFA II funds and will be subject to periodic review of their performance against planned milestones.

Other PDUFA II projects (e.g., CBER's EDR and CDER's COMIS Redesign) are currently being defined and scoped and will be incorporated into this plan and reviewed by the TRB in the 1st quarter of FY 1999. Funds for development of these projects will not be released until 1) a business case supporting the project has been submitted to the OCIO and 2) the project has been reviewed through the ITBP process.

Other PDUFA II items not associated with a specific project or which support multiple projects may be reviewed independently by the OCIO to ensure compliance with Agency best practices and architecture standards.

4.2 Independent Review

Following reauthorization of PDUFA, Five-Year Funding Plans covering PDUFA-related IT and personnel requirements were submitted by PDUFA-related FDA organizations for approval by the Deputy Commissioner for Management and Systems. The Deputy Commissioner for Management and Systems directed that the Office of Human Resources and Management Services (OHRMS) and the OCIO work collaboratively to review and assess the economic soundness of each PDUFA Center/Office's PDUFA II Five-Year Plan. To that end, OHRMS worked with OFM and with the Centers/Offices to review the non-IT portions of the plans, and OCIO engaged the services of an independent contractor to work directly with the PDUFA Centers/Offices to assess the IT portions of the five-year plans. This section documents the process employed to conduct the IT review and presents the results achieved based on the analysis.

The submitted spending plans from CBER, CDER, and ORA collectively totaled in excess of $107 million over the five-year planning horizon, or about 14.5 percent of the fees to be collected for the PDUFA II period.

The independent review process was accomplished by conducting a series of meetings with appropriate IT and other management personnel from each organization to discuss the underlying assumptions, and the derivation and support for each PDUFA II budget line item. Each session was designed to:

- Provide an open forum for mutually exploring opportunities to conserve resources (e.g., by reducing redundancies and inconsistent assumptions among the centers);
- Ensure a fair and consistent distribution of IT funding among the affected PDUFA II organizational units, and
- Guarantee that funding requests were driven by supportable business requirements.

A special effort was made to identify areas where the addition of funding to the originally submitted budgets would be both appropriate and beneficial from a business need perspective.

The primary focus of this independent review was to assure budget soundness in the Centers/Offices plans. If essential resource components were not identified in the plans, additions were made. By mutual

agreement between OCIO and the Centers/ORA, some budget line items were deleted and some resources were reduced.

The result of the independent review was a proposed budget plan (termed the "Proposed PDUFA II Five-Year IT Budget Plan") for each Center/Office for spending PDUFA II dollars between FY 1998 and FY 2002. This Proposed Five-Year PDUFA II IT Budget Plan, which totals $103 million, was reduced from the original submissions of $107 million. A further "temporary reduction", termed a "reserve" has been defined, which initially reduces the Proposed Five-Year PDUFA II IT Budget Plan from $103 million to $86.6 million. The "reserve" funds will be set aside for access by the PDUFA Centers/Offices when appropriate business conditions have been satisfied. ERSR Program costs are provided in Appendix D.

- *"Proposed PDUFA II Five-Year IT Budget Plan" Additions* – Among the largest additions included funding CDER and CBER Plans to provide electronic access by ORA's field investigators from approximately 50 sites (e.g., 21 District Offices, the larger Resident Post Offices, several Labs and selected smaller Resident Post locations). Other additions are as follows:

  - CBER: Infrastructure changes (e.g., cabling, network switches, servers, storage and other hardware and software), laptop requirements, and a new pre-market label data repository.
  - ORA: Funding for desktops and laptop equipment required by field offices and investigator personnel;
  - OIRM: Funds for expected PDUFA II electronic submission enhancements to the recently installed EDI gateway, and funds for contractor assistance to help with the Agency's major evolution in data architectures which is required to achieve a paperless environment by 2002; and funding for Phase 1 of Information Infrastructure Architecture (ISA) training, installation and networking requirements as these directly relate to the PDUFA II user base;
  - CBER and CDER: Funds for Independent Validation and Verification for Year 2000 and/or FDAMA needs at both CDER and CBER for systems that relate directly to PDUFA II.

- *"Proposed PDUFA II Five-Year IT Budget Plan" Reductions* – All Center and ORA original plan submissions were not consistent with standard ISA cost planning assumptions (for example, for workstations, monitors, servers, and required software), and thus, the funding requested in the plans was reduced. Where appropriate to the Agency, generally-accepted IT replacement lifecycles were adopted (e.g., monitors) which also reduced funding requirements. Further, personnel (FTE) expenses that had been included in the IT plans were removed. Other major reductions were developed from tighter re-estimates by the Centers of their new development and training needs.

- *Reserves* – During the reviews, six crucial IT projects were identified as being in such a formative stage of their development as to preclude definitive estimates of actual funding requirements, as well as, an accurate assessment of investment timing, that will be needed for their completion. Therefore, to assure adequate future funding for these six mission-critical priorities, center-specific reserves have been earmarked accordingly within the *Proposed Five-Year PDUFA II IT Budget Plan*. Portions of the reserve will require detailed analysis to understand the justification before release of funds will be approved. Working in close cooperation with the PDUFA organizations, these funds will be released for use by an organization when 1) a business case supporting the additional expenditures has been submitted to OCIO and 2) the project has been included in the IT Business Planning process.

Overall, the proposed PDUFA II Five-Year IT Budget Plan represents a sound, appropriate PDUFA II budget for IT-related investments. It reinforces and supports the Agency's drive to a largely paperless, pre-market approval environment by the year 2002 as required by the reauthorized PDUFA II legislation.

4.3 "Reserve" Management

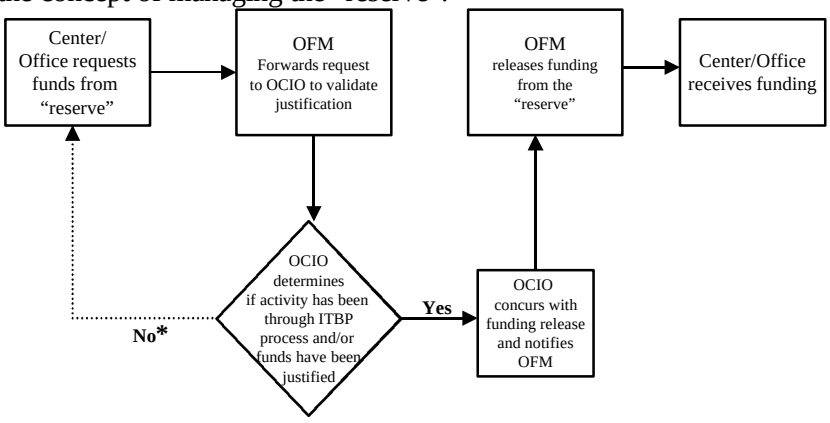
During the initial independent review, funds for certain IT projects were placed in a "reserve" because these projects were considered to be in such a formative stage of their development as to preclude definitive estimates of actual funding requirements. These reserve funds will be managed by a collaborative effort between the Centers/ORA, OCIO, and the Office of Financial Management (OFM).

When a Center/Office identifies a need for funds to be released from their "reserve" budgets, they will send OFM a funding request. OFM will forward the request to OCIO, requesting notification that the activity is in the PDUFA Information Management Five-Year Plan and is approved for funding. OCIO will verify that the activity for which funding has been requested has been through the IT Business Planning process or that the activity has been justified by an independent review by OCIO to ensure compliance with Agency best practices and architecture standards.

If the activity is in the PDUFA Information Management Five-Year Plan and has been reviewed, OCIO will issue notification to OFM to release the funds. If the activity is not in the PDUFA Information Management Five-Year Plan or has not been reviewed through the IT business planning process, the requesting Center/Office will be notified by OCIO of the requirements needed for funds to be released. Requirements may include any or all of the following activities:

- Preparation of a business case or update of an existing business case;
- Review by the TRB; and/or
- An independent assessment by OCIO of non-project related activities.

Figure 4 presents the concept of managing the "reserve".



*Center/Office will be notified that their activity will have to be reviewed and/or justified in order for funds to be released

Figure 4

APPENDIX A

DESCRIPTION OF CURRENT MAJOR CDER ERSR PROJECTS[5]

1. Electronic Document Room (EDR)
   (credentialed by the TRB)

2. Division File System (DFS)
   (credentialed by the TRB)

[5]CDER is developing the business case for the COMIS Redesign Project. A business case for this project will be completed by 1st quarter of FY 1999 and subsequently reviewed by the TRB.

1. Electronic Document Room (EDR) *(credentialed by the TRB)*

Business Need

CDER must provide the capability and capacity for electronic receipt and archive of electronic regulatory submissions. Ultimately, CDER's EDR will support receipt and archive of all regulatory submissions, including full New Drug Applications (NDAs), Abbreviated New Drug Applications (ANDAs), Investigational New Drugs (INDs), Drug Master Files, Annual Reports, OTC Monographs, etc.

IT Solution

CDER established the EDR in FY 1997 to accommodate the receipt, archive, and storage of electronic Case Report Forms (CRFs) and Case Report Tabulations (CRTs) for New Drug Applications (NDAs). CDER has published Industry Guidance for submitting CRFs and CRTs without an accompanying paper copy. These CRFs and CRTs are being received in the EDR as text images in PDF format for archive.

Submissions come in to the EDR on one of several physical media types:

- Microsoft MS-DOS formatted 3 ½" diskettes
- ISO 9660 CD-ROMS
- 8mm DLT tape created on VMS and NT systems

The EDR currently handles data submitted on 3 ½" PC formatted diskettes or on ISO standard CD-ROMs on Windows 95 workstations. Data submitted on 20/40 DLT tapes is loaded directly on the VMS server or through the NT server's tape drive. Because CDER expects that there may be some sponsors who will submit applications by paper for the foreseeable future, the Center must continue to accommodate paper information flow.

The EDR equipment is located at CDER's Central Document Room (CDR). The equipment currently includes:

- an Alpha VMS server with a CD-ROM drive and a 20/40 DLT tape drive;
- a Windows 95 workstation with a CD-ROM drive (a CD-ROM changer and a 4mm DAT drive may be added at a later date);
- an INTEL Windows NT 4.0 server with a CD-ROM drive, a 20/40 DLT tape drive and running the Microsoft Internet Information Server (IIS) with Microsoft Frontpage Extensions; and
- at least one COMIS workstation.

The CDR is connected to the CDER VMS cluster in the Parklawn Building through a T1 communications line. Large datasets are moved manually to 20/40 DLT tapes. The shares which hold the electronic CRFs and CRTs may be located on the CDER cluster or on a server drive in any building that is part of the CDER wide area network. Below is a listing of the desktop and network components of the EDR system:

Desktop:
Pentium desktop computers with Windows 95, Pathworks, Documentum, TCPIP, Microsoft Networking, Microsoft Office 95.

Network:
Digital Alpha and VAX servers running OpenVMS, Digital Alpha servers running Microsoft Windows NT, and Intel processor servers running Microsoft Windows NT

Benefits

Beneficiaries of the EDR project will be reviewers in CDER who will have electronic access to submissions. Plans include providing electronic access to this information to field offices within the Office of Regulatory Affairs (ORA). Regulated industry will benefit from an easier and faster submission process.

EDR will provide capability and capacity to receive and archive electronic submissions in accordance with the ERSR Program goals. The EDR will reduce overall costs of the document room contract and reduce the storage requirements. Target reductions in paper submissions are 25 percent in FY 1998, 50 percent in FY 1999, and 75 percent in FY 2000.

2. Division File System (DFS) *(credentialed by the TRB)*

Business Need

An Electronic Document Management System (EDMS) is a critical component of the Electronic Regulatory Submission and Review (ERSR) program. The goal of ERSR is to provide the capability and capacity for processing electronic regulatory submissions and reviews by the year 2002. The goal of EDMS is to provide an easy to use, automated means for creating, managing, electronic signature, and archiving internally generated documents pertaining to the IND/NDA review process. Within CDER, DFS is the application that meets the primary functional requirements of an EDMS. DFS makes it possible for CDER reviewers to file reviews electronically and access historical data and consult reviews on-line from their desktops rather than relying on paper copies. DFS greatly reduces manual filing, distribution, and data entry processes, thereby reducing the administrative burden on reviewers. In addition, DFS reduces data errors by having data automatically transferred to the Center-Wide ORACLE Management Information System (COMIS) rather than having it re-keyed and provides an electronic repository for internally generated documents.

IT Solution

DFS provides for the creation, management, electronic signature, and archiving of internally generated review documents. DFS is being planned and implemented in two phases with each phase consisting of one increment each. Phase 1 (electronic repository) is currently being deployed. Phase 2 (additional functions such as updating COMIS) is under development.

The Decision Support System (DSS), a critical component of CDER's EDMS, was planned and implemented in one phase that consisted of three increments. Increment 1 (Windows-based interface to COMIS) has been deployed although performance improvements and other enhancements are currently being incorporated. Increment 2 (graphical Report of Assignments) was beta tested, however, the user group had concerns about visibility of the data and requested holding off on its deployment. Increment 3 (integration of DSS with other components) was completed and is operational.

DFS was first piloted in the Division of Oncology using LinkWorks but the pilot was unsuccessful. Based on an extensive tool study, Documentum was selected as a replacement and approved by CDER's IT Coordinating Committee (ITCC). Another pilot was conducted in Oncology using Documentum and it was successful. DFS is now operational in one new drug review divisions and offices. DFS will be rolled out to the remaining new drug review divisions by the end of calendar year 1998.

Benefits

Primary beneficiaries will be IND/NDA reviewers in CDER, as well as the Center's FOI Staff who will use DFS as their document management system. Regulated industry will benefit from speedier access to status information and ultimately faster turnaround on IND and NDA reviews. The public will benefit because new safe and effective drugs will reach the marketplace sooner. DFS provides the following benefits:

- Management Information: DFS supports a core business function of the Center—the review and approval of INDs and NDAs. DFS will provide management with up-to-the-minute information about the new drug review process. DFS answers critical questions such as the reviews that have been completed for a particular submission, the reviewers' analyses and recommendations, who has signed off on a review, whether a related review was written, and the status of a particular submission in the review process.

- Technology: DFS is in alignment with the rest of the Center's and Agency's technology investments, including its technical infrastructure and core applications. DFS supports the Agency's focus on moving toward a paperless environment.

Appendix B

DESCRIPTION OF CURRENT MAJOR CBER ERSR PROJECTS

1. Electronic Document Room (EDR)
(To be reviewed by the TRB in the 1st quarter of FY 1999)

2. Regulatory Management System (RMS)
(Credentialed by the TRB)

1. Electronic Document Room (EDR) *(To be reviewed by the TRB in the 1st quarter of FY 1999)*

Business Need

CBER must provide a capability to accommodate receipt and archive of electronic submissions in order to comply with the FDA Modernization Act (FDAMA). Ultimately, CBER's EDR will support receipt and archive of Product License Applications (PLAs), Biologics License Applications (BLAs), Investigational New Drugs (INDs), Pre-market Approvals (PMAs), Pre-Market Notifications (510(k)s), New Drug Applications (NDAs) and Abbreviated New Drug Applications (ANDAs).

IT Solution

Currently, no definitive IT solution exists for CBER's Electronic Document Room (EDR). CBER has funded a requirements study to determine the specific requirements and high-level design needed for an Electronic submission system, including the feasibility of an Electronic Document Room which will be designed to accommodate PLAs, BLAs, INDs, PMAs, 510(k)s, NDAs and ANDAs.

CBER established a storage system within the central Document Control Center in the early 1990s to receive various electronic submissions and in FY 1997 began the receipt, archive, and storage of electronic Case Report Forms (CRFs) and Case Report Tabulations (CRTs) for Product License Applications (PLAs). These CRFs and CRTs are being currently received as text images in PDF format for review and storage.

Submissions come in to CBER on one of several physical media types:

- Microsoft MS-DOS formatted 3 1/2" diskettes
- ISO 9660 CD-ROMS

Equipment located in CBER's Woodmont Office Center (WOCI) LAN Room handles data submitted on 3 1/2" PC formatted diskettes or on ISO standard CD-ROMs. The equipment currently includes an Alpha NT 4.0 server with a CD-ROM drive running the Microsoft Internet Information Server (IIS) with Microsoft Front page Extensions with connections to a DLT tape back-up unit and a CD-ROM Tower.

WOCI is connected to the CBER VAX cluster in the Parklawn Building through a T1 communications line. Dark fiber is planned for FY 1999. The shared drives which hold the electronic CRFs and CRTs are located on a server drive in the Woodmont Office Center building that is part of the CBER wide area network.

Below is a listing of the desktop and network components of the interim system:

Desktop:
Pentium desktop computers with Windows 95, Pathworks, Documentum, TCP/IP, Microsoft Networking, Microsoft Office 95.

Network:
Digital Alpha server running Microsoft Windows NT, and Intel processor servers running Microsoft Windows NT

Benefits

Beneficiaries of the EDR project will be reviewers in CBER who will have electronic access to submissions. Regulated industry will benefit from an easier and faster submission process. EDR will provide capability and capacity to receive and archive electronic submissions in accordance with the ERSR program goals. Specific costs and benefits will be delineated in the requirements analysis to be delivered in late September 1998.

2. Regulatory Management System (RMS) *(Credentialed by the TRB)*

Business Need

The Regulatory Management System (RMS) initiative fully supports the Center for Biologics Evaluation and Research's (CBER's) information technology strategic plan. Specifically, it supports the following goals:

- A managed and integrated regulatory process from discovery through postmarketing
- Interactive information systems that are integral to all CBER activities.

The RMS initiative also supports the transition to an electronic regulatory environment, in compliance with the Reinventing Government (ReGO) Initiatives and the Paperwork Reduction Act of 1995 as well as the FDA Modernization Act (FDAMA) and Prescription Drug User Fee Act II (PDUFA) goals and CBER non-PDUFA milestones.

IT Solution

The RMS initiative supports these goals and objectives by providing:

- A data structure supporting the integration of data from discovery through postmarketing
- Migration of existing data from legacy systems to the new data structure
- Application software for data tracking and retrieval in support of CBER business functions from discovery through postmarketing, including strategic information needs identified by CBER's Information and Data Committee and Managed Review Committee "to-be" processes
- Application software to track and report on PDUFA and non-PDUFA milestones and other target dates
- Application software to generate, store, and route electronic review-related documents and comments
- Enhanced tracking of industry submissions, including automated routing for review
- Enhanced submission review of reference materials.

The RMS initiative has a positive impact on the supported business processes. This initiative will increase business process efficiency and improve quality through a variety of means. It will provide a more complete data set that enables rapid retrieval of business-critical data. It will implement Agency and Center data and process standards that improve data/document quality and consistency, as well as technical (hardware and software) standards that provide the most user-friendly and supportable interface possible. The RMS initiative will provide a single user interface and seamless integration across applications to further ensure efficient use and will enable rapid access to business-critical documents through an integrated interface to industry and FDA documents. The initiative also will enable access to integrated data and electronic documents generated during product and facility reviews, as well as the collection of statistics on milestones and workload for greater management and accountability.

Commercial-off-the-shelf (COTS) alternatives evaluated to provide capabilities similar to RMS are documented in a Document Management/Workflow study conducted in CBER in 1995. Documentum, which is widely used in the pharmaceutical industry, was chosen based on user needs and technical specifications.

The RMS initiative is an information management system that includes an Oracle database and Documentum docbase. The program includes data migration protocols, utilities, and client/server software applications. The primary investment in RMS thus far has consisted of analyses of regulatory review functions most appropriate for RMS support and implementation of RMS release 1.2 in the second quarter of FY 1998. An integrated database design and BLA subsystem design were also completed. RMS 1.2 couples the existing BIMS IND legacy data base with a pilot Documentum application on approximately 50 desktops. Extensive functionality is available for recording, importing and subrouting Clinical Trials, access to clinical trial outlines and data, searching and displaying amendment types and viewing telecons.

Whereas RMS 1.2 is focused on the review of INDs and the corresponding data base, RMS 2.0, scheduled for October, 1998, offers an integrated database for all legacy data as well as the new Biologics License Application

(BLA) and the re-engineered business process. The RMS 2.0 database will also support the replacement of legacy systems such as CCS and DLS within a new Document Accountability and Tracking System (DATS). When implemented in 10/98, RMS 2.0 will also replace the establishment licensing, product licensing and lot release modules of the current Biologics Regulatory Management System (BRMS).

The implementation plans to support these functions include piloting electronic document management, developing an integrated database and migrating legacy data, designing an application architecture, developing a prototype system, and fielding the first component of a production system to an initial group of users.

The scope of RMS includes all industry submissions from discovery through postmarketing and associated data and document tracking, routing, and retrieval.

The RMS technical approach emphasizes project planning and management; a phased development approach based on strategic priorities, rapid application development, stakeholder/customer involvement and buy-in throughout the development process; and the use of Agency and Center Information Technology (IT) standards.

The RMS initiative depends on FDA Information Systems Architecture (ISA) standards and other directives implemented through CBER's Infrastructure Improvement Project and the CBER standard desktop rollout. Similarly, the following are dependent upon the completion of the RMS initiative:

- Achievement of PDUFA goals;
- Implementation of a single, harmonized license application form;
- Issuance of a single license for all biological products;
- The Electronic Freedom of Information Act (EFOIA);
- M2 Electronic Gateway; and
- Progress towards the implementation of the Paper Reduction Act.

Some factors are critical to ensuring the successful deployment of the RMS. These include funding/contract vehicles, continued management support in terms of establishing priorities, defining CBER submission review policy, and providing staff resources.

Benefits

The RMS initiative provides strategic, operational, management information, and technology benefits. The strategic value is difficult to quantify but substantial. RMS is the main technology vehicle to meet PDUFA mandates and to provide a seamless information system to support the regulatory review process. The RMS architecture can support application requirements that change over time and emphasizes modular development and phased implementation.

The RMS integrated databases, coupled with seamless and uniform RMS application software, allow for efficient data entry and data query and enhance the overall quality and consistency of data throughout the regulatory life cycle. When fully implemented, RMS will provide CBER managers with vital information on numerous core activities. RMS is strongly aligned with the FDA's systems strategy and technology base. Moreover, RMS directly supports CBER's strategy of migrating to a single, integrated database as the foundation for future software applications.

The major stakeholders, beneficiaries, and customers of the RMS initiative include industry sponsors and manufacturers, CBER management at Center and Office levels, CBER review and administrative staff at the Division and Branch levels, Document Control Center (DCC) staff, and FOI staff. Secondary beneficiaries of this initiative will be Office of the Commissioner (OC) and ORA personnel as well as CDRH and CDER for those premarket applications undergoing joint review.

APPENDIX C

DESCRIPTIONS OF CURRENT MAJOR AGENCY/CROSS-CUTTING ERSR PROJECTS

1. Agency Technical Monitoring and Support
(TRB Review not applicable)

2.0 EDI Gateway
(Release 1.0 and Release 2.0 – Requirements Analysis credentialed by the TRB)

3.0 ORA Support
(TRB Review not applicable)

4. ISA and Central Infrastructure Support
(TRB Review not applicable)

1. Agency Technical Monitoring and Support *(TRB Review not applicable)*

Business Need

The FDA Modernization Act (FDAMA) of 1997 requires the Agency to improve its efficiency through the application of information technology. Specifically the Act directs FDA to:

- Develop and update its IT infrastructure to allow, by FY2002, the paperless receipt and processing of electronic submissions
- Establish and maintain an information system to track the status and progress of each application or submission (including petitions, notifications, or other similar forms of requests) submitted to the Agency for action
- Meet new BLA/NDA review performance goals, add new classification codes, and identify new regulatory procedures that will necessitate changes to existing information systems.

One important provision of the Act is the reauthorization of the Prescription Drug Users Fee Act of 1992 (PDUFA II). PDUFA II provides users fees to be collected from the drug and biologics industry. These fees are in turn targeted to improve FDA review of pre-approval drug and biologic applications, establishment licensing, and other services. In order to ensure that user fee resources are properly managed, the Deputy Commissioner for Management and Systems (OMS) directed OCIO facilitate the development of an Agency PDUFA II Information Management Five-Year Plan. This plan must contain the IT requirements of all key Agency stakeholders, CBER, CDER, ORA, and OIRM and be consistent with each Center/Office's Five Year plan.

IT Solution

In order to ensure FDA is meeting the IT requirements of FDAMA, an annual review of the ERSR project will be conducted. The consultants will compare programmatic planning documents and other related material (from CBER, CDER, ORA, and OIRM) with the ERSR Business Cases to identify any inconsistencies, synergies and make efficiency recommendations to senior management. In addition to planned reviews, oversight will include coordination and support of data management. This data management can include consultant support for Agency-level data modeling and data dictionary development.

There is no technical solution associated with this effort.

Benefits

The Agency as a whole will benefit from this oversight by gaining an assurance that PDUFA IT Plans are founded on IT industry best practices. This assurance should results in sound budgetary decisions, lower project costs, and improved information re-use.

Information gathered during this independent review can be used in development of the IT investment portfolio, for out-year budget formulation, and for miscellaneous data calls from the Department.

External stakeholders who share a vested interest in the consistent, proper spending of PDUFA dollars include:

- Industry sponsors and manufacturers – reduced paper costs and manpower to compile paper submissions; better access to status information through the use of secure e-mail; ultimately faster turnaround on reviews
- Public – a more efficient review that will expedite marketplace availability of new drugs and biologics

2. EDI Gateway *(Release 1.0 and Release 2.0 – Requirements Analysis credentialed by the TRB)*

Business Need

The recent passage of the FDA Modernization Act of 1997 coupled with the renewal of Prescription Drug User Fee Act (PDUFA II) require that the Agency improve its review efficiency and productivity. Specifically, they require the Agency to transition its review environment into a "paperless" environment by completing three high level integrated steps:

1. Providing industry guidance and standards for electronic filing of submissions;
2. Providing standard capability for receiving electronic submissions from industry; and
3. Reinventing internal processes and systems that accommodate electronic reviews.

IT Solution

The Electronic Data Interchange (EDI) Gateway represents an Agency solution for satisfying Step Two. The purpose of the Gateway is to place a centralized, Agency-wide Gateway into day-to-day operations for receiving regulatory submissions securely. The main functions of the Gateway are to receive submissions, decrypt those that are encrypted, authenticate that the submission is genuine, acknowledge to the sender that the submission was received, maintain an audit log of gateway actions, and make the submission available to the proper Center for regulatory processing.

This strategic investment has been designed in a scaleable manner to facilitate the adaptation for all potential electronic submission types of the Agency. This adaptation will take place over time as resources become available and technology solutions advance. The initial phase, Release 1.0, of the system was designed to support drug adverse event reports for CDER. This phase was designed and built based on requirements and validation from an Agency-wide expert working group consisting of representatives from CDER, CBER, CDRH, CVM, and OC. The initial release has passed acceptance testing and awaits two critical external milestones: 1) Full production implementation of AERS and 2) Regulated Industry's ability to submit ICH standard drug adverse events.

Release 2.0 of the Gateway will be designed to support pre-approval submissions identified under the renewal Prescription Drug User Fee Act (PDUFA II). Initially, the Agency will coordinate Gateway resources to support ERSR and coordinate all development in concert with the rollout of electronic submission guidance documents. This schedule will be coordinated with CDER and CBER. The estimated milestone schedule and costs are highly dependent on the outcome of the Release 2.0 requirements analysis.

Lastly, the Gateway is intended to serve as a central utility function for the entire Agency. Its development has helped to foster technical information sharing within the Agency and improved the FDA's IT leadership reputation with Regulated Industry.

Benefits

From a strategic standpoint, the Gateway represents a technology resource that will be refined to support the needs of the PDUFA program and then leveraged to other components of the Agency. For example, the lessons learned and technology solutions from the implementation of a paperless environment in CBER and CDER can be applied to other non-PDUFA Centers and result in common or shared technology solutions that benefit the Agency as a whole.

EDI may vastly reduce the paperwork associated with processing reports for both the Agency and regulated industry. EDI also has the potential to decrease reporting costs to the FDA and drug companies. Processing electronic transactions is expected to result in significant cost and resource reductions for both the Agency and industry.

3. ORA Support *(TRB Review not applicable)*

Business Need

ORA's current practice for Field Office communication with CDER can involve large volumes of paper at times. Generally, every district office receives a copy of the Chemical Manufacturing Controls (CMC) section (Field Copy) of a marketing submission directly from the manufacturer. Labs receive methods validation documentation directly from CDER. Investigators review this paper in order to perform pre-approval inspections and post-approval Good Management Practices (GMP) inspections. In addition, investigators must access information from Drug Master Files stored at CDER about active pharmaceutical ingredients and ancillary facilities that are used in support of approval of NDAs and ANDAs. Also the Biomedical Research Monitoring (BIMO) investigators need access to information in NDAs concerning animal studies and human clinical trials, and in ANDAs concerning bioequivalence studies. The ORA users include (but are not limited to) the pre-approval managers, the lab chemists, the Compliance Officers, investigators, and the CSO. The number of users varies from one in a resident post to twenty in a district office. Documents are usually reviewed by the offices before an inspection.

Because ORA's business requirements will impact the design considerations of the projects within the ERSR Program, CDER and CBER will incorporate ORA's needs into their system development life cycle. At least each regional office, district office and some large resident posts could need direct electronic access to the electronic documents maintained by CDER and CBER to be able to browse and search for the applicable documents. For resident posts not directly on the network and for users on inspection trips, remote access capability needs to be provided. Moreover, tracking the status and progress of field assignments needs to be maintained.

IT Solution

An analysis of the changes required to ORA's computing infrastructure is planned. ORA envisions that they will need the capability to 1) provide each district office, each laboratory, some large resident posts on the network, and each regional office direct electronic access to the electronic documents maintained by CDER and 2) provide the ability to browse and search for the documents pre-authorized by CDER and download what they need when they need it. ORA does not require detailed access to CBER's BLA applications in the same context as in audits of CDER NDAs in accordance with CDER guidelines. One possibility is to provide a seamless dial-up capability to access the information they need and to have added electronic storage capability. Several Agency infrastructure changes now underway could address this such as FACTS, the new Agency security perimeter, etc. Other technology may be required consistent with the final design of ERSR.

Benefits

CBER, CDER, and ORA will benefit from incorporating ORA's needs into CBER and CDER's system development life cycle. ORA field offices' access to electronic documents will facilitate review of information in preparation for on-site inspections and investigations and will relieve some of the burden on the Centers of providing information in paper format.

4. ISA and Central Infrastructure Support *(TRB Review not applicable)*

Business Need

The current FDA IT environment consists of numerous layered and often incompatible product suites. Significant time and energy are expended in moving information throughout the Agency, to the industry it regulates, and to the general population that it serves. FDA has business needs that are not being consistently met by its current IT environment. This demands an IT infrastructure that:

- Improves communication;
- Enables collaboration;
- Increases productivity; and
- Creates a more manageable and cost effective environment.

PDUFA related activities are dependent upon successful implementation of the ISA. OIRM will coordinate ISA activities in conjunction with the implementation of PDUFA projects to ensure that IT standards are fully supportive of PDUFA activities.

IT Solution

The Information Systems Architecture initiative, coordinated by OIRM, will standardize the information systems architecture of the entire Agency beginning with the e-mail, the network operating system, and the desktop operating system. Components of the Baseline Infrastructure include:

- Office Automation Suite (Microsoft Office Pro 97);
- Electronic Messaging (Microsoft Exchange);
- Network Operating System (Microsoft NT); and
- Desktop Operating System (Windows 95).

Technical contacts have been established for each Center/Office, and detailed implementation plans tailored to each organization are being developed with Center/Office participation. OIRM will coordinate ISA activities for PDUFA Centers by providing technical support through the Network Control Center and other components of OIRM.

Benefits

Adopting a standardized IT infrastructure will substantially reduce the total life-cycle costs for PDUFA Centers and the Agency as a whole. A standardized IT infrastructure will improve the process of moving information throughout the Agency, to the industry it regulates and to the general population it serves while decreasing operations and maintenance costs, and decreasing training time and costs by providing users with applications with a common interface.

The ability to effectively deploy several key PDUFA systems (e.g., DFS and RMS) requires the IT infrastructure provided in Phase I of the ISA. Implementation of the Baseline Infrastructure will provide the Agency with the infrastructure necessary to comply with mandates and regulatory policies that indirectly support the PDUFA Program.

Appendix D

ERSR Program Costs

Budgeted Costs (in millions)

This section provides a breakdown of the costs (in millions) associated with the ERSR program. Additional non-IT related overhead costs associated with PDUFA activities in the Office of Management and Systems that will be identified and published in a separate plan.

Costs by Functional Area

The following three tables present ERSR program costs by ERSR functional area. These costs are presented by Center, by major component project, by life-cycle phase (where breakdown was available).

Electronic Submissions

Major Area		FY1998	FY1999	FY2000	FY2001	FY2002	TOTAL
CDER							
Electronic Document Room (EDR)	Development	1,198	1,135	540	550	560	3,983
	Hardware	1,287	1,287	1,326	0	0	3,900
	Software	30	0	0	0	0	30
	Total	2,515	2,422	1,866	550	560	7,913
Standards		150	190	190	190	190	910
Scientific Databases		514	735	790	515	385	2,939
O&M		1,800	1,550	1,525	1,525	1,525	7,925
CDER Total		**4,979**	**4,897**	**4,371**	**2,780**	**2,660**	**19,687**
CBER							
Electronic Document Room (EDR)	Analysis	700	0	0	0	0	700
	Development	447	197	97	47	47	835
	Development & Maintenance	0	500	200	200	200	1,100
	Integration with RMS	0	1,100	1,100	1,600	1,600	5,400
	Total	1,147	1,797	1,397	1,847	1,847	8,035
Standards		256	256	256	256	256	1,280
O&M		50	100	100	0	0	250
CBER Total		**1,453**	**2,153**	**1,753**	**2,103**	**2,103**	**9,565**
ORA							
Electronic Submissions Activities		165	120	88	96	96	565
O&M		0	73	225	405	455	1,158
ORA Total		**165**	**193**	**313**	**501**	**551**	**1,723**
OIRM							
EDI Gateway	Requirements Analysis	150	0	100	0	100	350
	Development	0	500	0	100	0	600
	Project Management	60	120	81	85	89	435
	Hardware Support	15	17	20	22	25	99
	Software Support	60	60	15	18	20	173
	Operations & Maintenance	43	43	0	0	0	86
	Total	328	740	70	72	80	1,290
OIRM Total		**328**	**740**	**70**	**72**	**80**	**1,290**
Total Electronic Submissions		**6,925**	**7,983**	**6,507**	**5,456**	**5,394**	**32,265**

Information/Document Managing and Tracking

Major Area		FY1998	FY1999	FY2000	FY2001	FY2002	TOTAL
CBER							
Regulatory Management System (RMS)	Development	3,450	1,750	1,100	600	500	7400
	O&M	158	109	17	17	17	318
	Total	3,608	1,859	1,117	617	517	7718
O&M		495	350	325	200	200	1570
Other		125	150	175	100	100	650
CBER Total		**4,228**	**2,359**	**1,617**	**917**	**817**	**9938**
CDER							
COMIS Redesign	Development	872	1,922	1,300	502	502	5098
	O&M	350	350	350	400	400	1850
	Total	1,222	2,272	1,650	902	902	6948
O&M		250	350	300	250	250	1400
Other		300	225	123	24	25	697
CDER Total		**1,772**	**2,847**	**2,073**	**1,176**	**1,177**	**9,045**
ORA							
EDMS Software		0	11	11	11	21	54
ORA Total		**0**	**11**	**11**	**11**	**21**	**54**
OIRM							
Agency Technical Monitoring and Support		110	270	280	280	280	1220
OIRM Total		**110**	**270**	**280**	**280**	**280**	**1,220**
Total Information/Document Managing and Tracking		***6,110***	***5,487***	***3,981***	***2,384***	**2,295**	**20,257**

Other Electronic Initiatives

Major Area		FY1998	FY1999	FY2000	FY2001	FY2002	TOTAL
CBER							
Technical Infrastructure		1525	2112	1723	1210	1023	7593
Technical Support		390	400	400	400	400	1990
Training		129	134	100	134	134	631
CBER Total		**2044**	**2646**	**2223**	**1744**	**1557**	**10214**
CDER							
Division Files System (DFS)	Analysis	100	200	120	120	120	660
	Development	1,654	1,404	1,404	904	904	6270
	O&M	0	250	350	350	350	1300
	Total	1,754	1,854	1,874	1,374	1,374	8230
Technical Infrastructure		2,349	1,926	1,889	1,489	1,525	9,178
Technical Support		445	520	535	540	545	2,585
Training		450	450	450	100	100	1,550
CDER Total		**4,998**	**4,750**	**4,748**	**3,503**	**3,544**	**21,543**
ORA							
Technical Infrastructure		360	269	257	257	395	1,538
Training		0	4	4	4	4	16
ORA Total		**360**	**273**	**261**	**261**	**399**	**1,554**
OIRM							
ISA and Central Infrastructure Support		0	437	314	0	0	751
OIRM Total		**0**	**437**	**314**	**0**	**0**	**751**
Total Other Electronic Initiatives		***7,402***	***8,706***	***7,546***	**5,508**	**5,500**	**34,062**

Cost Summary by Center

The following three tables present a summary of the ERSR program costs by ERSR functional area, by Center/Office. These tables are followed by a table displaying the grand totals for the ERSR Program for each Center/Office.

Electronic Submissions Summary

Electronic Submissions		FY 1998	FY 1999	FY 2000	FY 2001	FY2002	Total
CBER	Proposed	1,453	2,153	1,753	2,103	2,103	9,565.0
	Reserve	0	0	0	0	0	0.0
CDER	Proposed	4,979	4,897	4,371	2,780	2,660	19,687.0
	Reserve	0	0	0	0	0	0.0
ORA	Proposed	165	193	313	501	551	1,723.0
	Reserve	0	0	0	0	0	0.0
OIRM	Proposed	328	740	70	72	80	1,290.0
	Reserve	0	0	390	740	390	1,520.0
Totals	Proposed	6,925	7,983	6,507	5,456	5,394	32,265.0
	Reserve	0	0	390	740	390	1,520.0

Information/Document Managing and Tracking Summary

Information/Document Managing and Tracking		FY 1998	FY 1999	FY 2000	FY 2001	FY2002	Total
CBER	Proposed	4,228	2,359	1,617	917	817	9,938.0
	Reserve	150	700	1,100	1,100	1,200	4,250.0
CDER	Proposed	1,772	2,847	2,073	1,176	1,177	9,045.0
	Reserve	0	1,000	1,500	250	250	3,000.0
ORA	Proposed	0	11	11	11	21	54.0
	Reserve	0	0	0	0	0	0.0
OIRM	Proposed	110	270	280	280	280	1,220.0
	Reserve	0	0	0	0	0	0.0
Totals	Proposed	6,110	5,487	3,981	2,384	2,295	20,257.0
	Reserve	150	1,700	2,600	1,350	1,450	7,250.0

Other Electronic Initiatives Summary

Other Electronic Initiatives		FY 1998	FY 1999	FY 2000	FY 2001	FY2002	Total
CBER	Proposed	2044	2646	2223	1744	1557	10,214.0
	Reserve	0	0	0	0	0	0.0
CDER	Proposed	4,998	4,750	4,748	3,503	3,544	21,543.0
	Reserve	939	1,620	1,169	1,385	1,375	6,488.0
ORA	Proposed	360	273	261	261	399	1,554.0
	Reserve	0	0	0	0	0	0.0
OIRM	Proposed	0	437	314	0	0	751.0
	Reserve	0	0	0	0	0	0.0
Totals	Proposed	7,402	8,106	7,546	5,508	5,500	34,062.0
	Reserve	939	1,620	1,169	1,385	1,375	6,488.0

Total Summary By Center/Office

NOTE: Funds have been included in CBER and CDER budgets and are earmarked for incorporating ORA requirements in their respective Centers. These funds are also considered to be in "reserve," and ORA must concur with the use of these funds before they are released.

Grand Totals		FY 1998	FY 1999	FY 2000	FY 2001	FY2002	Total
CBER	Proposed	7,725	7,158	5,593	4,764	4,477	29,717.0
	CBER funded ORA requirements*	75	125	100	75	75	450.0
	Reserve	150	700	1,100	1,100	1,200	4,250.0
CDER	Proposed	11,749	12,494	11,192	7,459	7,381	50,275.0
	CDER funded ORA requirements*	0	600	150	75	75	900.0
	Reserve	939	2,620	2,669	1,635	1,625	9,488.0
ORA	Proposed	525	477	585	773	971	3,331.0
	Reserve	0	0	0	0	0	0.0
OIRM	Proposed	438	1,447	664	352	360	3,261.0
	Reserve	0	0	390	740	390	1,520.0
Totals	Proposed	20,437	21,576	18,034	13,348	13,189	86,584.0
	Reserve**	1,164	4,045	4,409	3,625	3,365	16,608.0

*Funds were included in CBER and CDER's plans to cover costs associated with defining requirements and implementing technology for ORA's role in the ERSR Program.
**includes funded ORA requirements

Appendix E

Acronyms

Acronyms

AERS	Adverse Event Reporting System
AMF	Administrative Management of Files
ANDA	Abbreviated New Drug Applications
BA/BE	Bioavailability/Bioequivalency
BER	Blood Establishment Registration System
BIMO	Biomedical Research Monitoring
BLA	Biologic License Applications
BRMS	Biologics Regulatory Management System
CBER	Center for Biologics Evaluation and Research
CDER	Center for Drug Evaluation and Research
CDR	Central Document Room
CIO	Chief Information Officer
CMC	Chemistry, Manufacturing and Controls
COMIS	Corporate Oracle Management Information System
COTS	Commercial Off-the-Shelf
CRF	Case Report Form
CRT	Case Report Tabulations
CTD	Common Technical Documents
CVM	Center for Veterinary Medicine
DATS	Document Accountability and Tracking System
DCC	Document Control Center
DFS	Division File System
DIA	Drug Information Association
DMF	Drug Master File
DSS	Decision Support System
EDI	Electronic Data Interchange
EDMS	Electronic Document Management System
EDR	Electronic Document Room
EES	Establishment Evaluation System
EFOIA	Electronic Freedom of Information Act
ERS	Electronic Regulatory Submission
ERSR	Electronic Regulatory Submission and Review
EVA	Entry Validation Application
EWG	Expert Working Group
FACTS	Field Accomplishments and Compliance Tracking System
FDA	Food and Drug Administration
FDAMA	FDA Modernization Act
FOI	Freedom of Information
FTE	Full-time Equivalent
GPRA	Government Performance and Results Act
ICH	International Conference on Harmonization
IIS	Internet Information Server
IND	Investigational New Drug

IRM	Information Resources Management
ISA	Information Systems Architecture
IT	Information Technology
ITBP	Information Technology Business Planning
ITCC	IT Coordinating Committee
LERN	Library Electronic Reference Network
LRS	Lot Release System
M2	ICH M2 Expert Working Group (EWG) focusing on Electronic Standards for Transmission of Regulatory Information
M4	ICH M4 EWG focuses on Common Technical Documents (CTD) for the technical content of sections of the NDA
MIS	Management Information System
NDA	New Drug Application
NOS	Network Operating System
NPR	National Performance Review
OC	Office of the Commissioner
OHRMS	Office of Human Resources and Management Services
OIRM	Office of Information Resources Management
OMS	Office of Management and Systems
ORA	Office of Regulatory Affairs
PDF	Portable Data Format
PDUFA	Prescription Drug User Fee Act
PhRMA	Pharmaceutical Research and Manufacturers of America
PLA	Product License Applications
RAC	Regulatory Affairs Committee
RMS	Regulatory Management System
TBD	To Be Determined
TCP/IP	Transmission Control Protocol/Internet Protocol
TRB	Technical Review Board